

WHAT IS CLAIMED IS:

1. A polynucleotide sequence comprising:
 - (a) a first nucleotide sequence comprising a sequence selected from the group consisting of:
 - (i) a sequence encoding the p110 subunit of PI 3-kinase protein, and
 - (ii) a sequence encoding a derivative or mutant of (i) having a single or multiple nucleotide substitution, deletion or addition, said derivative or mutant having an activity of the p110 subunit of PI 3-kinase protein, and
 - (b) a second nucleotide sequence comprising a sequence encoding a cell membrane targeting sequence, said second nucleotide sequence being attached to the 5' or 3' end of said first nucleotide sequence.
2. A polynucleotide sequence of claim 1, wherein said first nucleotide sequence further comprises an additional sequence selected from the group consisting of :
 - (i) a sequence encoding a portion of the p85 subunit of PI 3-kinase protein that is capable of binding the p110 subunit of PI 3-kinase protein, and
 - (ii) a sequence encoding a derivative or mutant of (i) having a single or multiple nucleotide substitution, deletion or addition, said derivative or mutant being capable of binding the p110 subunit of PI 3-kinase.
3. A polynucleotide sequence of claim 2, wherein said additional sequence comprises the iSH2 domain of the p85 subunit of PI 3-kinase protein.
4. A polynucleotide sequence of claim 1 wherein said cell membrane targeting sequence is selected from the group consisting of
 - (a) a myristylation cell membrane targeting sequence, and
 - (b) farnesylation and palmitoylation cell membrane targeting sequences.

5. A sequence of claim 3, wherein said first nucleotide sequence comprises a sequence encoding p110* and said second nucleotide sequence comprises a sequence encoding a cell membrane targeting sequence selected from the group consisting of:

- (a) a myristoylation sequence and
- (b) farnesylation and palmitoylation sequences.

6. A polynucleotide sequence comprising:

(a) a first nucleotide sequence comprising a sequence selected from the group consisting of:

- (i) a sequence encoding the p110 subunit of PI3 kinase protein, and
- (ii) a sequence encoding a derivative or mutant of (i) having single or multiple nucleotide substitutions, deletions or additions, said derivative or mutant having an activity of the p110 subunit PI 3-kinase,

(b) a second nucleotide sequence comprising a sequence selected from the group consisting of:

- (i) a sequence encoding the iSH2 domain of the p85 subunit of PI3 kinase protein that is capable of binding the p110 subunit of PI 3-kinase protein, and
- (ii) a sequence encoding a derivative or mutant of (i) having a single or multiple nucleotide substitution, deletion or addition, said derivative or mutant being capable of binding the p110 subunit of PI 3-kinase protein, wherein said second nucleotide sequence is attached to a linker nucleotide sequence encoding a linker, said linker nucleotide sequence being attached to the 5' end of said first nucleotide sequence and forming a first fusion sequence, and

(c) a third nucleotide sequence encoding a cell membrane targeting sequence, attached to the 5' or 3' end of said first fusion sequence.

7. A polynucleotide sequence of claim 6 wherein said cell membrane targeting sequence comprises a sequence selected from the group consisting of:
 - (a) a myristylation cell membrane targeting sequence and
 - (b) farnesylation and palmitoylation cell membrane targeting sequences.
8. A cell transformed with said polynucleotide sequence of claim 1.
9. A cell transformed with said polynucleotide sequence of claim 6.
10. A transgenic fly comprising a transgene having a polynucleotide sequence of claim 6 under regulatory control of an eye specific promoter, wherein said fly exhibits a phenotypic change in eye morphology from normal to rough eye morphology.
11. A method of screening for an inhibitor of PI 3-kinase comprising:
 - (a) administering a candidate inhibitor to a transgenic fly of claim 10,
 - (b) observing any reversion in phenotype to normal eye morphology in said fly, said reversion being indicative of PI 3-kinase inhibitor activity.
12. A method of reducing cell death due to trauma, comprising administering to a mammalian patient a viral or non-viral vector comprising a polynucleotide sequence of claim 1.
13. A method of reducing cell death due to trauma, comprising administering to a mammalian patient a viral or non-viral vector comprising a polynucleotide sequence of claim 6.
14. A method of making a 3' phosphorylated inositol phospholipid comprising:
 - (a) contacting a purified p110 or p110* polypeptide with a vesicle including a PI 3-kinase substrate selected from the group consisting of phosphatidylinositol (PI), phosphatidyl 4-phosphate (PI4P) and phosphatidylinositol 4,5 bisphosphate (PI4,5,P2), and
 - (b) isolating a 3' phosphorylated inositol phospholipid.

15. A method of making a 3' phosphorylated inositol phospholipid comprising transforming a host cell with said polynucleotide of claim 1 and expressing said polynucleotide.

16. A method of making a 3' phosphorylated inositol phospholipid comprising transforming a host cell with said polynucleotide of claim 6 and expressing said polynucleotide.

17. A 3' phosphorylated inositol phospholipid made by the method of claim 14.

18. A 3' phosphorylated inositol phospholipid made by the method of claim 16.

19. A method of activating an enzyme effector of PI 3-kinase having a pleckstrin homology domain comprising:

(a) incubating a polynucleotide sequence of claim 1 with a 4' phosphorylated phosphatidylinositol selected from the group consisting of phosphatidylinositol 4 phosphate (PI4P) and phosphatidylinositol 4,5 bisphosphate (PI4,5P₂), to generate a mixture of 3' phosphorylated inositol phospholipids comprising phosphatidylinositol 3,4 bisphosphate (PI3,4P₂), and phosphatidylinositol 3,4,5 trisphosphate (PI3,4,5P₃),

(b) isolating a 3' phosphorylated inositol phospholipid of (a) and

(c) contacting an active polypeptide having a pleckstrin homology domain with an effective amount of said isolated 3' phosphorylated inositol phospholipid of (b).

20. A method of promoting activation in a mammalian patient of an insulin signaling pathway comprising contacting a cell characterized by insulin resistance with a vector comprising a polynucleotide sequence of claim 6.

21. A method of reducing cell death associated with trauma in a mammalian patient, comprising contacting a population of said patient's cells with an effective amount of a pharmaceutical composition comprising a 3' phosphorylated inositol phospholipid of claim 18.